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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/521,008	10/27/2005	Bart Van Den Hazel	0253us410	2777

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EXAMINER	
SEHARASEYON, JEGATHEESAN	
ART UNIT	PAPER NUMBER
1647	
MAIL DATE	DELIVERY MODE
04/07/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/521,008	VAN DEN HAZEL ET AL.	
	Examiner	Art Unit	
	Jegatheesan Seharaseyon, Ph.D	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 February 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18,20-40,42-47,50,51,56 and 59* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) *1-18,20-40,42-46,50,51 and 59* is/are allowed.

6)☒ Claim(s) *47 and 56* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *03 January 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/6/05 7 4/18/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This Office Action is in response to Applicant's election of Group I, Claims 1-18, 20-40, 42-47, 50, 51 and 59 drawn to an interferon-gamma polypeptide variant, nucleotides encoding such and a method of making without traverse filed 2/4/2008. The Office will join the method of treatment (claim 56) in the examination. Therefore, claims 1-18, 20-40, 42-47, 50, 51, 56 and 59 are pending and examined.

Information Disclosure Statement

2. The Information disclosure statements file 4/6/2005 and 4/18/2005 have been fully considered.

Drawings

3. The drawing filed 1/3/2005 are acknowledged.

Specification

4. The use of the trademark Actimmune (p.13), Tween (p.63), Pluronic (p.63) and Capsitol (p.65) etc. have been noted in this application. They should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner, which might adversely affect their validity as trademarks.

5. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code (p. 8 line 18). Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6a. Claim 47 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated or cultured cell comprising an expression vector, does not reasonably provide enablement for a host cell comprising an expression vector. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The Examiner has interpreted the claims as reading on isolated host cells, as well as host cells in the context of a multicellular, transgenic organism and host cells intended for gene therapy.

The specification discloses that "nucleotide sequence encoding an IFNG polypeptide of the invention in gene therapy applications" and both in vitro and in vivo gene therapy methodologies are contemplated (pg. 69). However, the specification does not teach any methods or working examples that indicate IFNG nucleic acid is introduced and expressed in a cell for therapeutic purposes. The disclosure in the specification is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. For example, the specification does not teach what type of vector would introduce the IFNG nucleic acid into the cell or in what

quantity and duration. Relevant literature teaches that since 1990, about 3500 patients have been treated via gene therapy and although some evidence of gene transfer has been seen, it has generally been inadequate for a meaningful clinical response (Phillips, A., J Pharm Pharmacology 53: 1169-1174, 2001; abstract). Additionally, the major challenge to gene therapy is to deliver DNA to the target tissues and to transport it to the cell nucleus to enable the required protein to be expressed (Phillips, A.; pg 1170, ¶ 1). Phillips also states that the problem with gene therapy is two-fold: 1) a system must designed to deliver DNA to a specific target and to prevent degradation within the body, and 2) an expression system must be built into the DNA construct to allow the target cell to express the protein at therapeutic levels for the desired length of time (pg 1170, ¶ 1). Therefore, undue experimentation would be required of the skilled artisan to introduce and express IFNG nucleic acid into the cell of an organism. Additionally, gene therapy is unpredictable and complex wherein one skilled in the art may not necessarily be able to introduce and express a IFNG nucleic acid in the cell of an organism or be able to produce a IFNG protein in that cell.

Due to the large quantity of experimentation necessary to introduce and express a IFNG nucleic acid in a cell of an organism for therapy, the lack of direction/guidance presented in the specification regarding how to introduce IFNG nucleic acid in the cell of an organism to be able produce that IFNG, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of transferring genes into an organism's cells, and the breadth of the claims which fail to recite any cell type limitations, undue experimentation would be

required of the skilled artisan to make and/or use the claimed invention in its full scope. (Please note that this issue could be overcome by amending the claims to recite, for example, "An isolated host cell…").

6b. Claim 56 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of interstitial pulmonary diseases, does not reasonably provide enablement for the prevention of the interstitial pulmonary diseases with the administration of IFNG polypeptide. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The factors to be considered when determining if the disclosure satisfies the enablement requirement have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breath of claims. Ex Parte Forman, (230 USPQ 546 (Bd. Pat. App. & Int. 1986); In re Wands, 858 F.2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988).

Claim 56 is drawn to the method of treatment or prevention of the interstitial pulmonary diseases by administering a composition of IFNG polypeptide. However, specification (pages 58-59) and prior art only teach the treatment of interstitial pulmonary diseases by the administration of IFNG. The specification as filed is insufficient to enable one of skilled in the art to practice the claimed invention for

prevention of the interstitial pulmonary diseases without an undue amount of experimentation because the specification and the prior art have not demonstrated the prevention of the interstitial pulmonary diseases by administering IFNG.

Applicant has not disclosed how to use the claimed invention for prevention of the interstitial pulmonary diseases by administering a combination of IFNG to the subjects. There is insufficient evidence of the invention with respect to the *in vivo* operability of the claimed invention. Specifically, specification and prior art only teach the treatment of interstitial pulmonary diseases and not the prevention of interstitial pulmonary diseases. For example, the specification fails to provide guidance with respect to what candidate population will be selected for the prevention of interstitial pulmonary diseases by administering IFNG of the invention. There is no disclosure in the specification with respect to the dosages required to obtain preventive effect. It is also unclear for how long one would have to administer the medication. It is noted that if a patient population with the "disease symptoms" are identified, the onset of disease has taken place, thus the pathology cannot be prevented (only further progression maybe stopped).

Since, there is inadequate guidance as to the nature of the invention, it is merely an invitation to the artisan to use the current invention as a starting point for further experimentation for the prophylaxis of interstitial pulmonary diseases by administering IFNG polypeptide of the invention. In addition, because there are no working examples provided describing prevention of interstitial pulmonary diseases or models it would

require an undue amount of experimentation to one of skill in the art to practice the claimed invention.

Given the breadth of claim 56 in light of the unpredictability of the art as determined by the lack of working examples, the level of skill of the artisan, and the lack of guidance provided in the instant specification and the prior art of record, it would require undue experimentation for one of ordinary skill in the art to make and use the claimed invention for the prevention of the interstitial pulmonary diseases by the administration of IFNG polypeptide.

Conclusion

7. The Office reviewed Applications 10/116,273, 10/195707, 10/130084 and 10/136, 495. The claims of the instant invention (with S132, S142, R137, R139 and R140) do not read on the allowed claims.

8. Claims 1-18, 20-40, 42-46, 50, 51 and59 are allowed. Claims 47 and 56 are rejected.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jegatheesan Seharaseyon, Ph.D whose telephone number is 571-272-0892. The examiner can normally be reached on M-F: 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath N. Rao, Ph. D can be reached on 571-272-0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

JS
March 31, 2008

/Jegatheesan Seharaseyon, Ph.D/
Primary Examiner, Art Unit 1647